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EXAMINER	
KELLY, ROBERT M	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,732	ZINN ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *124,126,127,163,164 and 166-175* is/are pending in the application.

4a) Of the above claim(s) *126 and 127* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *124,126,127,163,164 and 166-175* is/are rejected.

7)☒ Claim(s) *124,126,127,163,164 and 166-175* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendment of 2/16/10 are entered.

Claims 1-123, 128-162, and 165 are cancelled.

Claims 166-175 are newly presented.

Claims 125, 163, and 164 are amended.

Claims 124, 126, 127, 163, 164, and 166-175 are presently pending.

Election/Restrictions

It is noted that the presently pending claims all fall with the elected invention: that of Group VI, methods of treating inflammation by administration of a complement modulator, as elected in the election of 11/20/08. Moreover, the invention is considered with respect to the elected species, SEQ ID NO: 9, and Claims 126 and 127 remain withdrawn.

Claims 124, 126, 127, 163, 164, and 166-175 are considered with respect to SEQ ID NO: 9.

Note: Improper Amendment and Response

It is noted that Applicant's response is actually non-responsive for being improperly marked (e.g., Claims 126, 127, 163, and 164 are improperly marked to depend from Claim 124, because they depended thusly before, and Claims 126 and 127 should have been identified as "Withdrawn-amended" if they were amended). Such is technically non-responsive, however, the Examiner was able to note the true amendments, and as such, the improper amendment is forgiven this time.

In addition, Applicant has failed to identify which of the new claims, and amended claims, read on the elected invention and species, and as such, the response is not correct. However, this is forgiven, as the Examiner was able to determine which claims are presently pending and are drawn to elected invention.

Claim Status, Cancelled Claims

In light of the cancellation of Claims 1-123, 128-162, and 165, all rejections and/or objections to such claims are rendered moot, and thus, are withdrawn.

Specification

TITLE

The title is objected to for not refering to the claimed method.

ABSTRACT

The Examiner notes that thanks Applicant for filing a clean page containing the abstract.

Claim Objections

In light of the amendments to Claims 124 and 164, the objections to the various claims are withdrawn.

Claims 124, 126, 127, 163, 164, and 166-175 are objected to. Claim 124 recites that the complement modulator is expressed on the surface of the viral vector. However, while the Examiner himself understood what Applicant intends to claim, in actuality, the modulator is

displayed on the surface. In addition, the dependent claims do not alter this terminology, and hence, these claims are objected to for depending from an objected-to base claim.

Claim Rejections - 35 USC § 112 - clarity

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 124, 126, 127, 163, 164, and 166-175 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 124 recites "a viral vector comprising a complement modulator expressed on the surface of the vector". The metes and bounds are not clear. To wit, the vector is not "expressed" on the surface of the vector, but is displayed on the surface. Expression is the transcription, translation, and processing, and when this occurs, the viral vector is not a formed viral vector particle.

Claim 124 also recites "in gene therapy", and so it is not clear if a gene therapy protocol is required to take place, or if the claimed steps are what is required. Hence, the claim is not clear because it may or may not require other steps to be performed, essentially, it may be lacking essential method steps and/or structure, e.g., what is being treated by gene therapy, the gene(s) transferred, and how, etc. The claim is not clear for its scope.

Claims 126, 127, 163, 164, and 166-175 are rejected for depending from a rejected base claim(s) and not overcoming the lack of clarity in such base claim(s).

Claim Rejections - 35 USC § 112 – new matter, in gene therapy

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 163, 164, and 166-175 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for specifically encompassing NEW MATTER. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 124, given its broadest reasonable interpretation, appears to indicate that inflammation is reduced in any gene therapy protocol, by the claimed method, administered separately, as a separate vector. Note the rejection for clarity above. Such is determined to be specifically encompassed because the vector itself is not required to carry a transgene for any form of therapy, and the method appears to indicate that complement is inhibited simply by the vector, yet the claim specifically states "in gene therapy".

The depending claims are rejected for depending from the base claim and not overcoming the broad generic interpretation specifically encompassed.

Applicant's specification indicates that the vector itself is meant of the gene therapy protocols, as a proclaimed-new vector for use in gene therapy (e.g., paragraph 0116 of the Application Publication, as stated by Applicant's response).

However, given the only statements are to utilize it as the vector for affecting gene therapy, the Artisan would not have understood Applicant to have been in possession of the specifically encompassId secondary-to-gene therapy treatment, to reduce inflammation.

Therefore, the claims are properly rejected for comprising new matter.

Response to Argument – New Matter, "in gene therapy"

Applicant's response of 2/16/10 has been fully considered but is not found persuasive.

The Examiner has cited Applicant's quoted paragraph for support and provided a proper analysis and an effective rebuttal to the broad statement that the paragraph provides proper support.

Claim Rejections - 35 USC § 112 – New Matter, gene of interest

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 163, 164, and 166-175 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for claiming or specifically encompassing new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 170 has been presented to recite that the viral vector "comprises a gene of interest".

Because the other claims are the parent claim, or separately depending from the parent claim, they necessarily specifically encompass this limitation also.

Applicant cites paragraph 230 of the specification for the generic limitation provided.

However, such limitation is clearly limited to retroviral vectors, while the claims are not so-limited, and as such the paragraph does not provide support for a generic gene of interest.

Still further, the same limitation is within the disclosed framework of paragraphs 224-242 of the same Application Publication, and it is clearly indicated that the "gene of interest" is limited to a "reporter", and not to any sequence (e.g., paragraph 225).

Therefore, the Artisan would not have understood Applicant to have been in possession of the claimed invention at the time of filing, and therefore the claims are properly rejected for embracing or specifically encompassing new matter.

Response to Argument – New Matter, "gene of interest"

Applicant's response of 2/16/10 has been fully considered but is not found persuasive.

The Examiner has cited Applicant's quoted paragraph for support and provided a proper analysis and an effective rebuttal to the broad statement that the paragraph provides proper support.

Claim Rejections - 35 USC § 112 – new matter, targeting motifs

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 163, 164, and 166-175 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for claiming or specifically encompassing new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 171 requires the viral vector to comprise a targeting motif. The other claims are parent to, depend from 171, or depend separately from the same parent claim, Claim 124, and hence, specifically encompass such.

Applicant cites paragraph 140 (sic) for support. It is assumed that Applicant meant to recite paragraph 104. However, 104 is limited to adenoviral vectors with targeting motifs.

Still further, the specific motifs are supported by the same averred paragraph, as well paragraphs 105-108. It is noted however, the such paragraphs are also limited to adenoviral vectors.

Hence, the Artisan would not have understood Applicant to have been in possession of the invention as claimed, for the generic viral vectors encompassed.

Therefore, the claims are properly rejected for claiming or encompassing specifically, the invention as claimed.

Response to Argument – New Matter, "targeting motif[s]"

Applicant's response of 2/16/10 has been fully considered but is not found persuasive.

The Examiner has cited Applicant's quoted paragraph for support and provided a proper analysis and an effective rebuttal to the broad statement that the paragraph provides proper support.

Claim Rejections - 35 USC § 112 – limitations of claims 173 and 175

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 163, 164, and 166-175 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for specifically claiming or encompassing new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 173 and 175 encompass generic reporters, and CAR binding site mutants or ablation of integrin binding, to a generic viral vector.

The balance of the claims are generic as being the parent claim or separately-depending from the parent claim.

Applicant cites paragraphs 108-109, to support the promoter. However, such paragraph is clearly that the promoter is limitated within the context of paragraphs describing adenoviral targeting of inflammation (e.g., paragraph 106).

Applicant cites paragraph 118 to support the CAR binding site mutants, as well as ablation of integrin binding. However, such paragraph is similarly limited to adenovirus.

Hence, the Artisan would not have understood Applicant to have been in possession of the generic invention claimed at the time of invention.

Therefore, the claims are properly rejected for claiming or specifically encompassing new matter.

Response to Argument – New Matter, claims 173 and 175

Applicant's response of 2/16/10 has been fully considered but is not found persuasive.

The Examiner has cited Applicant's quoted paragraph for support and provided a proper analysis and an effective rebuttal to the broad statement that the paragraph provides proper support.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 124, 163, 164 under 35 U.S.C. 112, first paragraph, for lacking a fully-enabled scope, are withdrawn.

To wit, the claims as now drafted, no longer recite or are required to recite, a promoter.

I. Base Rejection: retroviral vectors with a generic complement inhibitor on its surface. This demonstrates the non-allowability of the broad claim as compared to the various species.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 124, 170, 171, and 173 remain and/or are newly rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,643,770 to Mason, et al., for reasons of record.

Mason teaches transforming tissues *in vivo* (e.g., Summary of the Invention), with retroviral vectors with gp70 envelope glycoproteins (e.g., Id., paragraph 3) which are chimerically expressing complement inhibitors (Id.), e.g., those found in pathogens (CIMs) (e.g., BACKGROUND, V. Inhibitors of the Complement System). In addition the vector which is administered is a retroviral vector (Summary of the Invention), and can have the gene encoding the gp41-CIM in the genome and linked to the expression control sequence (e.g., Id., paragraph 1, applicable to new claims 170, 171 (as it targets the complement system), 173 (the specification teaches promoters)). Still further, if enablement is to be questioned, it appears that the claims encompass the same complement inhibitors (e.g., Claims 1 and 8, and definition of "complement inhibitor" in specification, paragraph preceding Section IV., The Complement System), and still further, Claim 13, compared to Claim 14, demonstrates that Claim 13 specifically encompasses *in vivo* administrations. In addition, the use of a transgene for gene therapy is taught (e.g., section "II. Gene Transfer for Gene Therapy"), which inherently requires a transgene connected to a promoter for expression, at least for the protein encoding sequences described in the same section.

Response to Argument – 102(b), Mason

Applicant's argument of 2/16/10 has been fully considered but is not found persuasive.

Applicant argues that Mason teaches expression of the complement inhibitors in cells, from which the producer cells are derived, and therefore, it is the target cell that is designed to inhibit complement (pp. 11-13), and hence, Mason does not teach nor suggest reducing inflammation in gene therapy in a subject, comprising the administration of vectors displaying a complement inhibitor (Id.).

Such is not persuasive. The citations of Applicant's responses are directed to paragraphs teaching packaging of the viral vectors, which are taught in the specification to be subsequently used for administration. Moreover, the claims, as cited, clearly evidence that the viral vector displays the complement inhibitor (e.g., Claim 8), and specifically encompass gene therapy in vivo (e.g., Claim 14 compared to Claim 13, which depends from Claim 8). The field of the invention also states that these particles are for gene therapy. Moreover, the specification teaches that the inhibition acts on inhibiting inflammation (e.g., Section entitled "IV. The Complement System").

II. Modifications of the Retroviral Base Rejection to Utilize Adenoviral Vectors

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, and 170-173 remain and/or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., for reasons of record.

As shown above, Mason teaches expression of fusion proteins to place a complement inhibitor onto the surface of a retroviral vector and use to transform tissues. However, Mason does not teach the use of adenoviral vectors.

On the other hand, it is well known that adenoviral vectors suffer from complement-mediated inactivation (e.g., Xing, et al. (2001) Cell Research, 11(2): 116-24, figure 5B). Moreover, it is well known to link peptides to be displaced on the surface of an adenovirus (e.g., U.S. Patent No. 7,468,181 to Vogels, et al., paragraph 6 of the Detailed Description, describing the addition of peptides to several surface displayed proteins of adenoviruses).

Further, it is well known that adenoviral vectors contain other targeting motifs, e.g., in the knob, fiber, and penton bases. Moreover, Vogels teaches that Serotype 5 is common serotype of adenovirus which is utilized for transformations (e.g., Detailed description), and it contains an RGD motif. (For the sake of clarity, it is also Officially Noted that Adenovirus Type 5 is well known for gene therapy protocols.)

Hence, it would be obvious to modify the Mason to utilize adenoviral vectors. The Artisan would do so to provide adenoviral vectors for administration and avoid complement-mediated inactivation. Moreover, the Artisan would have had a reasonable expectation of success, as it was already to so-display peptides, and Adenoviruses are well known for gene delivery.

Response to Argument – 103(a), Mason, Xing, Vogels

Applicant's response of 2/16/10 has been fully considered but is not found persuasive.

Applicant argues that Vogels at best is direct to linking or fusing targeting moieties to a viral particle, and that Claim 124 requires the modulator to be expressed on the surface, and such is distinct (p. 14, penultimate paragraph).

Such is not persuasive. First, the scope of "expressed" is indeterminate, as it simply appears mean "displayed" on the surface (note the rejection for lack of clarity and commensurate objection, above). Second, the same paragraph clearly evinces disclosure of attachment of the "targeting" protein to the surface-displayed proteins of the adenovirus. Third, the same paragraph teaches "chimeric" fibers as one example. Lastly, the same paragraph states that "Persons of skill in the art of adenoviral vector targeting will be aware of all the different possibilities that are applied to deliver the adenoviral vectors to the cells of interest", which clearly infers that the leap to producing a chimeric surface-displayed protein is not all that great.

Applicant suggests that Mason is fatally flawed, failing to describe the surface-expressed complement inhibitor (pp. 14-15, paragraph bridging).

Such is not persuasive. It is claimed in the claims, and in addition, the brief description of the invention teaches it (4th paragraph from the end).

III. Modification of (II) to Utilize a Hypervariable Region

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, and 170-173 remain and/or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to claims 124, 163, and 170-173 above, and further in view of U.S. Patent No. 6,127,525 to Crystal, et al., for reasons of record.

As shown above, the various references make obvious the claims, except the aspect of utilizing a hypervariable region for inserting the peptide.

Crystal demonstrates that several hypervariable regions of adenovirus may be deleted and/or substituted with chimeric peptides (e.g., paragraphs 11-12 of the section titled "Chimeric Adenovirus Coat Proteins").

As such the Artisan would find the invention obvious over the art. The Artisan would modify the references as Crystal demonstrates that these regions are tolerant to changes and it would place the peptide on the surface of the virus. Moreover, the Artisan would have a reasonable expectation of success, as Crystal teaches it would work, and Mason teaches that the peptides would work to ameliorate the complement inactivation of the virus.

Response to Argument – 103, in view of crystal

Applicant's argument of 2/16/10 has been fully considered but is not found persuasive.

Applicant argues that Crystal fails to make up for the deficiencies in the base references (pp. 16-17, paragraph bridging).

Such is not persuasive. There are no such deficiencies.

IV. Modification of (II) or (III) to utilize ED1

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, and 169-173 remain and /or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al as applied to claims 124, 163, and 170-173 above (II), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34, for reasons of record; and

Claims 124, 163, and 169-173 remain and/or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., and U.S. Patent No. 6,127,525 to Crystal, et al., as applied to claims 124, 163, and 170-173 above (III), and further in view of Inal, et al. (2000) FEBS Letters, 470: 131-34, for reasons of record.

As shown above, the various references make obvious the invention in each case, except that the references do not teach or make obvious the ED1 domain.

On the other hand, Inal teaches that the ED1 domain of Sh-TOR inhibits complement and does so when isolated from the normal protein (e.g., ABSTRACT).

Hence, it would be obvious to modify the references to arrive at the invention. The Artisan would do so to inhibit complement inactivation of the virus. Moreover, the Artisan

would have a reasonable expectation of success, as Inal has shown that the peptide works out of context.

Response to Argument – 103, references in view of Inal

Applicant's argument of 2/16/10 has been fully considered but is not found persuasive.

Applicant argues that the Inal does not make up for the deficiencies in the base references (e.g., p. 18, second paragraph).

Such is not persuasive. There are no such deficiencies as shown above.

V. Modification of (IV) to Further Include a His-Tag

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, 167, and 169-174 remain and/or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., and Inal, et al. (2000) FEBS Letters, 470: 131-34 as applied to claims 124, 163, and 169-173 above (II), and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74, for reasons of record; and

Claims 124, 163, 167, and 169-174 remain and/or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al.

(2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., and Inal, et al. (2000) FEBS Letters, 470: 131-34 as applied to claims 124, 163, and 169-173, and further in view of Huang, et al. (2000) Protein Expression and Purification, 18: 169-74, for reasons of record.

As shown above, the various limitations are obviated, except that of utilizing a His-Tag.

However, it was well known in the Art that His-Tagged entities can be isolated utilizing the His-Tag (e.g., Huang, ABSTRACT). Such His-Tag can also be considered as encoded by a reporter NA, as it can be used to report the presence of the protein to which it is attached.

Hence, it would have been obvious to modify the invention to include a His-Tag. The Artisan would do so to provide for easier isolation of the viruses with such ED1 expressed on its surface. Moreover, the Artisan would have a reasonable expectation of success, as it was well known to use His-Tags to isolate entities with such His-Tag.

Response to Argument - 103(a), further in view of Huang

Applicant argues that Huang fails to overcome the problems with the base references (e.g., pp. 19-20, paragraph bridging).

Such is not persuasive. There are no such deficiencies.

VI. Modification of V to Utilize 2 ED1 Sequences and a Linker

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is noted that the following rejections rely upon Oh, et al., which is a reference under 102(a), and hence, may be sworn behind to overcome the rejection.

Claims 124, 163, 166, 167, and 169-174 remain and/or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., Inal, et al. (2000) FEBS Letters, 470: 131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124124, 163, 167, and 169-174 above, and further in view of Oh, et al., (2003) Immunology, 110: 73-79, for reasons of record; and

Claims 124, 163, 166, 167, and 169-174 remain and/or are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, U.S. Patent No. 7,468,181 to Vogels, et al., U.S. Patent No. 6,127,525 to Crystal, et al., Inal, et al. (2000) FEBS Letters, 470: 131-34, and Huang, et al. (2000) Protein Expression and Purification, 18: 169-74 as applied to claims 124, 163, 167, and 169-174, and further in view of Oh, et al., (2003) Immunology, 110: 73-79, for reasons of record.

As shown above, the various limitations are obviated, except the use of 2 ED1 sequences, linked by a linker.

On the other hand, Oh teaches that a duplicated ED1 domain provides increased inhibition of complement activation over that of a single ED1 domain (p. 76, col. 2, paragraph 2). In addition, the linker may be as little as a peptide bond, given the broadest reasonable interpretation, and also, Oh teaches that amino acid 27 is not important, but is necessarily present in their homodimer (p. 78, paragraph 1).

Hence, it would have been obvious to modify the references to utilize Oh's ED1 duplicated domain. The Artisan would do so to increase complement inhibition. Moreover, the Aritsan would expect success, as Oh teaches that complement inactivation is greater than single ED1 domains.

Response to Argument – 103(a) further in view of Oh

Applicant argues that Oh fails to overcome the deficiencies of the base references (pp. 22-23, paragraph bridging).

Such is not persuasive. There are no such deficiencies.

VI. Modification of (II) to Utilize an AAV vector (AAV vector in AdV envelope)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, 164, and 170-173 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to Claims 124, 163, and 170-173, further in view of Goncalves, et al. (2001) Virology, 288(2): 236-46, for reasons of record.

The rejection is maintained because there is no art for the Examiner to determine that an AAV genome, within an AdV envelope should not be, given its broadest reasonable interpretation, considered an AAV vector.

As shown above, the references obviate the claims, except the use of an AAV vector.

Goncalves, however, teaches encapsulation of AAV vectors into Adenoviral envelopes, to thereby allow superior prolonged transgene expression and allowing larger inserts (e.g., ABSTRACT). Moreover, the transgenes for packaging from adenovirus are entered into the AAV genome (e.g., ABSTRACT).

Hence, it would have been obvious to make the invention as claimed. The Artisan would do so to increase the the time of transgene expression and allow larger inserts than AAV enveloped AAV vectors. Moreover, the Artisan would expect success, as Goncalves teaches it can be done.

Response to Argument – 103(a), further in view of Goncalves

Applicant argues that Goncalves does not make up for the deficiencies of the base reference(s) (p. 23, paragraph 2).

Such is not persuasive. There is no such deficiency.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124, 163, 170-173, and 175 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,643,770 to Mason, et al., Xing, et al. (2001) Cell Research, 11(2): 116-24, and U.S. Patent No. 7,468,181 to Vogels, et al., as applied to Claims 124, 163, and 170-173, above, and further in view of U.S. Patent No. 7,256,036 to Legrand, et al.

As shown above, the various aspects of the claims are obvious, except for the presence of a mutation in a CAR binding site.

On the other hand, Legrand teaches adenoviral vectors for use in gene therapy, which are modified in their CAR binding sites (e.g., Claim 1, "abolishing the capacity of said adenovirus for binding to the natural cellular receptor"; Brief Summary, paragraph 25, indicating that the natural cellular receptors encompass the receptor for CAR; and the concluding paragraph indicating that insertion of new ligands can redirect affinity to other cell types). Further mutation of the penton base can remove binding to integrins (e.g., paragraph 9 of the Breif summary). Doing so can remove normal tropism, allow the Artisan to modify the tropism with new targeting ligands (e.g., Id.).

Hence, it would be obvious to modify the CAR binding region or remove the integrin-biding region. The Artisan would do so to redirect targeting to distinct cell types and remove natural targeting. Moreover, the Artisan would expect success, as Legrand teaches such.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633